The Controversy Over the Prostate Specific Antigen Test

Prostate cancer screening with the prostate specific antigen (PSA) test among adult men is common in the United States. In Washington State, 69% of men over age 50 reported ever having been screened with PSA, and 48% reported PSA testing within the past year (2001-2002 Behavioral Risk Factor Surveillance System data for Washington State). While prostate cancer screening is widely practiced, routine screening is not recommended in most clinical guidelines. Most organizations (including the American Cancer Society, the American College of Physicians, and the American Urological Association) recommend informing men about the benefits and risks associated with prostate cancer screening, and having men decide with their physicians whether or not to be screened.

In order to understand why screening with the PSA test is controversial, we summarize the current literature about the PSA test in light of five criteria that are widely used to justify cancer screening tests.[1] There is good evidence to satisfy the first two criteria, but there is still much debate about PSA screening's sensitivity and specificity (criterion 3). Randomized controlled trials of prostate cancer screening are currently being conducted, and their results will answer questions about whether screen-detected prostate cancer is more curable than clinically-detected prostate cancer and whether PSA screening improves health outcomes.

1. The disease must constitute a significant public health problem.

- Prostate cancer is the most common non-skin cancer and the second most common cause of cancer death in American men.[2]
- There were approximately 29,900 deaths from prostate cancer in 2004.[3]

2. The disease must be identified in an asymptomatic, localized phase.

- In the screening arm of the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO), 88% of the men diagnosed with prostate cancer with PSA between 4 and 10 ng/mL had clinically localized disease. Men with higher PSA levels (> 10ng/mL) were more likely to have clinically advanced disease.[4]

3. The screening test must have appropriate sensitivity, specificity, and predictive value.

- Currently, PSA is considered abnormal if greater than 4.0 ng/mL.
    - A study of men in the Prostate Cancer Prevention Trial detected prostate cancer in 15.2% of men with PSA < 4.0 ng/mL.[5]
    - There is currently debate about lowering the PSA threshold for biopsy, which would increase sensitivity of the PSA test, but would also lower specificity.[6-8]
- An analysis of several studies of PSA screening resulted in average sensitivity of 71%, specificity of 75%, and positive predictive value of 37%.[9]
- A statistical study of PSA screening which corrected for verification bias resulted in sensitivity of 18% for men under 60 years old, which means that this test would miss 82% of prostate cancers with PSA > 4.0 ng/mL as threshold for biopsy.[7]

4. The potential for cure must be greater among screen-detected patients.

- Randomized controlled trials of prostate cancer screening are currently being conducted in the United States and Europe, but we will not know the results for several more years.[4, 10]
- A randomized controlled trial of treating prostate cancer with radical prostatectomy (RP) v. watchful waiting was completed in 2000. The two groups did not differ in all-cause mortality, but men in the RP group had a lower risk of death from prostate cancer. However, very few of the men in this trial (5%) had prostate cancer that was diagnosed via screening.[11] The two groups reported similar well-being and quality of life.[12]

5. There must be demonstrable improved health outcomes related to screening.

- As noted above, we are still awaiting evidence from randomized controlled trials on whether men who are screened for prostate cancer survive longer than those who are not screened.
- The majority of men with prostate cancer die from other causes,[9] but PSA does not distinguish between latent cancers (those that are slow-growing and unlikely to cause symptoms or illness) and aggressive cancers.[4]
- Prostate cancer treatment has several significant side effects, including sexual dysfunction and urinary incontinence. In one study, 80% of the men who had been treated with radical prostatectomy reported erectile dysfunction, and 49% reported urinary incontinence.[12] In another study, sexual dysfunction was reported by 50 – 60% of prostate cancer survivors, and urinary function problems were 8 – 27% of the same group (ranges reflect different types of cancer treatment).[13] Finally, a study of men in the Prostate Cancer Outcomes Study revealed that 71% of prostate cancer survivors reported erectile dysfunction and 14% reported urinary incontinence 5 years after being treated with radical prostatectomy.[14] The high rates of these serious side effects contribute to the controversy of screening for prostate cancer.

In light of the unknowns about ultimate risks and benefits of PSA screening and treatment for prostate cancer, several professional organizations recommend that men discuss prostate cancer screening with their physicians. Men should make an informed decision whether or not to screen for prostate cancer with their physicians (please see *Prostate Cancer Screening and Informed Decision Making*). While this literature review focuses on the PSA test, many of the same issues apply to prostate cancer screening with digital rectal examination, which is also widely practiced. As findings from the randomized controlled trials are published, clinical guidelines will change to reflect the evidence.

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Prepared by:

Peggy Hannon, PhD, MPH
Alliance for Reducing Cancer, Northwest
University of Washington Health Promotion Research Center

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